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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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NOVOZYMES BIOTECH, INC.
1445 DREW AVE
DAVIS, CA 95616

EXAMINER	
MARVICH, MARIA	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 06/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/710,760	ROYER ET AL.	
	Examiner	Art Unit	
	Maria B Marvich, PhD	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *90-94,97-100,103 and 104* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) *90-93* is/are allowed.

6)☒ Claim(s) *94 and 97-100* is/are rejected.

7)☐ Claim(s) *103 and 104* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to an Amendment filed 3/8/04. Claims 1-89, 95-96 and 101-102 have been canceled. Claims 103 and 104 have been added and claim 97 had been amended. Claims 90-94, 97-100 and 103-104 are pending in this application.

Response to Amendment

Any rejection of record in the previous action not addressed in this office action is withdrawn. There are no new grounds of rejection herein and therefore, this action is final.

Claim Objections

Claims 103 and 104 are objected to under 37 CFR 1.75 as being substantial duplicates of claim 94. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). It is unclear that the trichodiene synthase of claim 94 from *Fusarium venenatum* strain ATCC 20334 differs from the trichodiene synthase encoded by SEQ ID NO: 1 and from the trichodiene synthase contained in pTri5. SEQ ID NO: 1 and pTri5 are both obtained from *Fusarium venenatum* strain ATCC 20334 and therefore should be the same trichodiene synthase of claim 94 from *Fusarium venenatum* strain ATCC 20334.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 103-104 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **This is a new rejection necessitated by applicants' amendment.**

Claims 103-104 are vague and indefinite in that the metes and bounds of " the synthase having the amino acid sequence of SEQ ID NO: 2" are unclear. It is unclear if the term "having" is intended to be open or closed language. If it is closed then it is unclear how the synthase of claims 103-104 differs from that previously recited in claim 91, which recites "the synthase consisting of amino acids of SEQ ID NO: 2".

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 94 and 100 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This rejection is maintained for reasons of record in the office action filed 10/6/03 and restated below.**

Since the specific *Fusarium venenatum* cells deposited at ATCC 20334 are essential to the claimed invention, they must be obtainable by a repeatable method set forth in the

specification or otherwise readily available to the public. The invention does not recite use of any cells but instead specifically claims *Fusarium venenatum* cells deposited at ATCC as strain ATCC 20334. The *Fusarium venenatum* cells deposited at ATCC as strain ATCC 20334 are commercially available, however, commercial availability is not necessarily evidence that the public will have access to the material for the life of a patent (see MPEP 2404.01) (emphasis added). Others deposited the Fusarium venenatum of the invention, their availability in an unrestricted form for the life of a patent issued on the instant application cannot be ensured. Applicants must therefore deposit the specific *Fusarium venenatum* recited in the claims and thus satisfy the deposit requirement under 37 CFR 1.801-1.809.

Response to Arguments- Deposit Requirement

Applicants traverse the preceding rejection under 35 U.S.C. 112, first paragraph, on pages 7-8 of the amendment filed 3/8/04. Applicants argue that the *Fusarium venenatum* cells deposited at ATCC with deposit #20334 are known and readily available to the public as evidenced by the ATTC catalog and the ATTC web site which both list *Fusarium venenatum* cells ATCC 20334. 54 FR 34880 state that the examiner need not be unduly concerned about continued access to the public unless there is a reasonable basis to believe that the biological material will cease to be available during the life of the patent, the examiner should accept current availability as satisfying the requirement. And MPEP 2404.01 further teaches that the office will accept commercial availability as evidence that a biological material is known and readily available only when evidence is clear and convincing that the public has access to the material.

Applicant's arguments filed 3/8/04 have been fully considered but they are not persuasive. Applicants do not recite any *Fusarium venenatum* cell. Rather applicants recite specifically *Fusarium venenatum* cells deposited at ATCC under #20334. As applicants have not deposited the cells tehmselves, commercial availability cannot be guatanteed for the life of the patent should the cells be withdrawn from the open collectin by the original depositors. Public access during the term of the patent may affect the enforceability of the patent. Furthermore, any cells derived from the deposited cells cannot be guaranteed to be the same as those originally deposited and thus cannot beguaranteed to convey the same properties on the protein of the claim as the deposited strain. For example, the claims can be read as product by process claims, encompassing embodiments where the protein is directly obtained from the deposited strain. Any modifications of the protein is conveyed by the deposited strain would potentially be lost over time in strains derived from the deposited strain over time. Therefore, to ensure that the cells are available for the life of the patent, applicants must deposit the cells themselves.

Claims 97-100 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. **This rejection is maintained for reasons of record in the office action filed 10/6/03 and restated below.**

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the patent coupled with information known in the art without undue experimentation (*United States v. Telectronics, Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988)).

Whether undue experimentation is required is not based on a single factor but is rather a conclusion reached by weighing many factors (See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter, 1986) and In *re Wands*, 8USPQ2d 1400 (Fed. Cir. 1988); these factors include the following:

1) Nature of invention. The invention recites an isolated functional fragment of the trichodiene synthase of SEQ ID NO: 2 wherein one or more amino acids are deleted from the amino and/or carboxyl terminus of SEQ ID NO: 2. This invention utilizes disciplines of recombinant technology as well as protein production. As well, assays for "functional fragments" from among the recombinant molecules are required.

2) Scope of the invention. The fragments can have any number of deletions at the N-terminus or C-terminus. Therefore, claims 97-100 recite a broad collection of proteins.

3) Number of working examples and guidance. While the sequence of SEQ ID NO: 2 is taught in the specification, no examples of fragments of trichodiene synthase or what domains or regions are required for function of trichodiene synthase. Therefore, there is no indication of a structure-function relationship between the sequence of SEQ ID NO 2 and trichodiene synthase activity. Furthermore, the instant specification fails to demonstrate any examples or specific guidance for the identification or isolation of "functional fragments" of SEQ ID NO: 2, i.e. assays for the analysis of trichodiene fragments that would meet the limitations of the claims. Applicants simply state that using methods known in the art specific for the enzyme with reference to Hohn and Beremand, 1989 on page 31, line 3-8. This reference teaches the primary structure of a trichodiene synthase (TS) gene isolated from *Fusarium sporotrichiodes* (see abstract). This guidance, for the isolation and sequence analysis of trichodiene synthase genes is

provided in the specification. However, no guidance is given for the isolation of "functional" fragments of trichodiene synthase **protein**.

4) State of the art. Recombinant technology for the generation of new protein fragments is highly developed. However, the ability to determine *a priori* whether a mutation will generate a functional fragment is not. Therefore, the art must be considered to be poorly developed.

5) Unpredictability of the art. Without knowing the structure-function relationship of SEQ ID NO: 2, the ability to predict the effect of mutations on function is highly unpredictable.

6) Amount of Experimentation Required. The invention recites isolated functional fragments of trichodiene synthase. In view of the unpredictability of the art of predicting the functional nature of fragments of SEQ ID NO 2 deleted of any number of amino acids from the C-terminus and/or the N-terminus: undue experimentation would be required to practice the claimed methods with reasonable expectation of success, absent a specific and detailed description in the specification. Given the unpredictability of the art, the poorly developed state of the art with regard to predicting the structural/ functional characteristics of a protein from primary amino acid sequence alone, the lack of working examples and the lack of guidance provided by applicants, the skilled artisan would have to have conducted undue, unpredictable experimentation to practice the claimed invention.

Response to Arguments- lack of enablement

Applicants traverse the claims rejection under 35 U.S.C. 112, first paragraph, on pages 7-8 of the amendment filed 3/8/04. Applicants argue that a fragment having trichodiene synthase activity is defined in the specification as a polypeptide having one or more amino acids deleted

from the amino and/or carboxyl terminus and as such involve simply removing one or more amino acids from the amino and/or carboxyl terminus of SEQ ID NO: 2. The resultant fragment can be assayed for trichodiene synthase activity. Applicants have submitted that similar fragments were considered allowable in Patent numbers 6,221,644, 6,372,464 and 6,489,154 which have similar disclosures as the instant case with only the explanation that "each application is reviewed on its own merits". Applicants are concerned that protection of the invention would be inadequate without reciting fragments of SEQ ID NO: 2.

Applicants' arguments filed 3/8/04 have been fully considered but they are not persuasive. The claims recite isolated functional fragments of trichodiene synthase. While the function of SEQ ID NO: 2 is understood to be trichodiene synthase, the ability to determine which of the fragments generated by the deletion of amino acids from the N and/or C-terminus is also functional is highly unpredictable due to the lack of guidance in the specification and prior art of record. By reciting that amino acids are deleted from the amino and/or carboxyl terminus of SEQ ID NO: 2, a large number of fragments of SEQ ID NO: 2 are possible that are deleted of any number of amino acids from the C-terminus and/or the N-terminus. Predicting the functional nature of any of these fragments is an unpredictable art. In the instant case, the office has shown that the specification does not provide the requisite enablement for the identification of fragments that are deleted of any number of amino and/or carboxyl terminus amino acids that possess trichodiene synthase activity. As to the patentability of the instant case in light of similar claims in published patents that possess similar disclosures, rejections based upon this argument have been addressed in *in re* Giolito and Hoffman. "It is immaterial whether similar claims have

been allowed to others" (see *in re* Giolito and Hoffman 188 USPQ 645). Rather, each application is reviewed on its own merits.

Claims 97-100 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This rejection is maintained for reasons of record in the office action filed 10/12/01 and 10/6/03 and restated below.**

Claim 97 is drawn to an isolated functional trichodiene synthase of SEQ ID NO: 2 wherein one or more amino acids are deleted from the amino and/or carboxyl terminus. Therefore, applicants claim a genus of functional trichodiene synthase molecule with any number of amino and/or carboxyl terminal deletions.

The written description requirement for genus claims may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with known or disclosed correlations between function and structure, or by a combination of such characteristics sufficient to show that the applicant was in possession of the claimed genus.

In the instant case, applicants teach full-length trichodiene synthase from *Fusarium venenatum*. The disclosure teaches that a fragment is a polypeptide having one or more amino acids deleted from the amino and/or carboxyl terminus. However, applicants do not teach any

fragments of trichodiene synthase or what domains or regions are required for functional trichodiene synthase. Therefore, there is no disclosure of a structure-function relationship between the sequence of SEQ ID NO 2 and trichodiene synthase activity. Given the large size and diversity of fragments generated by deletion at the N and/or C-terminus and the inability to determine which will also have the essential element, it is concluded that the invention must be empirically determined. In an unpredictable art, the disclosure of no species would not represent to the skilled artisan a representative number of species sufficient to show applicants were in possession of claimed genus.

Response to Arguments- lack of written description

Applicants traverse the claims rejection under 35 U.S.C. 112, first paragraph, on page 8 of the amendment filed 3/8/04. Applicants state that the arguments presented in Section V, in response to the rejection based upon lack of enablement, are sufficient to overcome the instant rejections.

Applicants' arguments filed 3/8/04 have been fully considered but they are not persuasive. While the function of SEQ ID NO: 2 is understood to be trichodiene synthase, the ability to determine which of the fragments generated by the deletion of amino acids from the N and/or C-terminus is also functional is highly unpredictable due to the lack of guidance in the specification and prior art of record. The simple deletion of amino acids at the C and/or N-terminus has the potential to generate a broad genus of fragments. The specification does not reduce to practice the ability to determine which fragments will also be "functional and the ability to determine *a priori* whether a mutation will generate a functional fragment is highly

unpredictable. A structure-function relationship for trichodiene synthase has not been provided. Therefore, the instant specification hasn't provided a structural/ functional basis for the skilled artisan to envision a broad genus of fragments that are deleted of amino and/or carboxyl terminus amino acids and still possess trichodene synthase activity.

Conclusion

Claims 90-93 are allowed.

Claim 94 and 97-100 are rejected.

Claims 95-96 are objected to as being duplicates of claim 94.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B Marvich, PhD whose telephone number is (571)-272-0774. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, PhD can be reached on (571)-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maria B Marvich, PhD
Examiner
Art Unit 1636

May 21, 2004

GERRY LEFFERS
PRIMARY EXAMINER